REMARKS

This responds to the Final Office Action dated August 4, 2010.

Claims 10, 31, 32, 37 and 42 are canceled without prejudice while claims 43-50 have been added. As a result, claims 2, 4, 8, 9, 28, 29, 30, 41, 43-49 and 50 are now pending in this application.

Claim 2 has been amended by incorporation of the subject matter of claims 31 and 32.

New claim 43 repeats the subject matter of claim 2 and includes the subject matter of canceled claim 42. The phrase "and killing said cell by cytotoxic T cell mediated cell killing" has been added to line 2 of this claim. Support for this language is present in lines 12-14 of claim 2. New claims 44-50 recite the language of claims 4, 8, 9, 28, 29, 30 and 41, but these claims depend from claim 43 (rather than claim 2).

Applicants submit that no new matter has been added to the application.

The Rejection of Claims under § 102

Claims 2, 4, 8-10, 28-32, 37 41, and 42 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by WO 96/07432. The Examiner asserts that WO 96/07432 is not limited to internalization of toxic molecules and, although WO 96/07432 does not state that the method disclosed therein results in cell surface expression of an antigen, the steps taught by WO 96/07432 would purportedly inherently result in such expression.

However, the method of claim 2 includes not only irradiation of a cell *ex vivo* to present an antigen on the surface of the cell but also administration of the cell back into the mammal. Nowhere does WO96/07432 describe such a method. The entirety of the WO96/07432 disclosure is drawn to transfer of molecules into the cytosol of cells with no teaching or recognition that the cells can become immunogens or the targets of cytotoxic T cell killing. Moreover, because WO96/07432 fails to recognize that antigen can be presented on the surface of a cell, WO96/07432 provides no motivation to administer cells containing such antigens to a mammal. In addition, the claims are drawn to methods involving cancer cells, and WO96/07432 fails to disclose any such methods for cancer cells.

The fact that WO96/07432 fails to disclose anything about administering cells to mammals, after *ex vivo* irradiation to present antigens on the cells' surface, is demonstrated by the text of WO96/07432 itself. For example, WO96/07432 discloses nothing about generating an immune response of any sort. In fact, the terms "antigen" and "T cell" do not appear anywhere in the text of WO96/07432. The word fragment "immun" appears only three times – each time in the context of transporting an immunoglobulin into the cytosol of a cell so that the immunoglobulin can treat or kill the cell. Nowhere does WO96/07432 disclose a method that includes irradiating a cell to cause presentation of an antigen on the surface of the cell followed by administration of the cell to a mammal, resulting in cytotoxic T cell mediated killing of the cell by a cytotoxic T cell specific for the antigen presented on the cell.

Similarly, the method of claim 43 includes both cell surface presentation of an antigen and killing of the cell by a cytotoxic T cell *in vitro*. However, WO96/07432 does not teach or suggest any *in vitro* method in which cytotoxic T cells are present to achieve the cell killing. As discussed above, the terms "antigen" and "T cell" appear nowhere in WO96/07432. Therefore, this claim is novel over WO96/07432.

In addition, both of independent claims 2 and 43 are drawn to methods involving cancer cells. However the teachings of WO96/07432 with respect to cancer cells are limited. On page 7, WO96/07432 describes only an in situ treatment of tumors – there is no mention of removing a cancer cell for any form of *in vitro* or *ex vivo* treatment. Thus, such disclosure by WO96/07432 fails to teach the *ex vivo* treatment and the administration of the cell back into the mammalian subject as described in Applicants' claim 2. Similarly, the WO96/07432 disclosure at page 7 fails to disclose removal of a cancer cell from a mammal, and the *in vitro* treatment specified in claim 43 (including the cytotoxic T cell killing of the cancer cell).

The *in vitro* cancer cell manipulations described in the Examples of WO96/07432 are limited to internalization of toxins (e.g., gelonin) and fail to mention anything about presentation of an antigen or cytotoxic T cell killing of the cancer cell. This disclosure therefore fails to anticipate Applicants' claim 43. Similarly, the administration of treated cancer cells to a mammal as recited in Applicants' claim 2 was not known, appreciated or contemplated before Applicants' invention.

Applicants submit that inherent anticipation cannot be founded upon the facts of this case. The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993) (reversed rejection because inherency was based on what would result due to optimization of conditions, not what was necessarily present in the prior art); *In re Oelrich*, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' "In *re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted) (The claims were drawn to a disposable diaper having three fastening elements. The reference disclosed two fastening elements that could perform the same function as the three fastening elements in the claims. The court construed the claims to require three separate elements and held that the reference did not disclose a separate third fastening element, either expressly or inherently.). Also, "[a]n invitation to investigate is not an inherent disclosure" where a prior art reference "discloses no more than a broad genus of potential applications of its discoveries." *Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1367, 71 USPQ2d 1081, 1091 (Fed. Cir. 2004) (explaining that "[a] prior art reference that discloses a genus still does not inherently disclose all species within that broad category" but must be examined to see if a disclosure of the claimed species has been made or whether the prior art reference merely invites further experimentation to find the species).

Here one of skill in the art would not recognize that the missing subject matter (inducing presentation of an antigen on a cell resulting in cytotoxic T cell mediated cell killing by a cytotoxic T cell specific for the antigenic peptide) was necessarily present in the WO96/07432 disclosure.

At best, the WO96/07432 provides no more than a broad genus of potential applications and fails to describe Applicants' claimed species. The entirety of the WO96/07432 disclosure is not applicable to cancer cells. For example, it is clear from the WO96/07432 disclosure that only certain types of molecules should be introduced into cancer cells. At page 7, WO96/07432 is

limited to introduction of photosensitizing agents and molecules for treatment of cancer (gelonin, antibodies, transferring, photsensitizers, apoB). The Examples are limited to introduction of toxins into cancer cells.

The Examiner points to WO96/07432 claims 2 and 12 as alleged evidence that WO96/07432 teaches that a variety of molecules are introduced into cancer cells. Claim 2 depends from claim 1, which is merely a generic method – it does not disclose the specific species of methods recited in Applicants' claims. Claim 12 depends from claim 9, which relates to a composition for the modification of neoplastic and other cellular processes that contains *inter alia* a "cellular process-modifying compound." The language "cellular process-modifying compound" indicates that the compound itself affects a cellular process and not that the cell acts on the compound to display it on the cell surface. Nowhere is cell surface presentation mentioned or suggested. Therefore, the only molecules falling within this scope must be those which have an effect internally, and in the case of a neoplasm, an antineoplastic effect (e.g., as recited in claim 10). The data relating to inhibition of protein synthesis in cancer cells by gelonin (e.g., in WO96/07432 FIG. 5) confirms this interpretation by teaching that the gelonin directly inhibits protein synthesis within the cell. Gelonin is not fragmented and presented on the cell surface – instead it is fully functional within the cytosol of the cell. FIG. 5 demonstrates that protein synthesis is inhibited within the cell. Thus, gelonin is acting only as a "cellular process-modifying compound." Gelonin is not acted on by the cell and then presented as a cell surface antigen. Nowhere does WO96/07432 contemplate introduction of cancer antigens into cancer cells that are presented in the cell surface of the cancer cell. One of skill in the art would understand from the Examples, including the data on gelonin inhibition of protein synthesis, that no cell surface presentation of antigens occurs.

Thus, one of skill in art would NOT conclude from the WO96/07432 that any cell surface presentation can take place. It is NOT clear that the missing descriptive matter is necessarily present in the WO96/07432 reference, and persons of ordinary skill in the art would NOT recognize that cell surface presentation can occur from the WO96/07432 disclosure.

In addition, even if WO96/07432 were somehow to teach surface presentation even those teachings would not destroy the novelty of Applicants claims because elements relating to the treated cancer cells being re-administered to a mammal (claim 2) and that cell killing is achieved

in vitro by cytotoxic T cells (claim 43) are entirely missing from the WO96/07432 disclosure, and cannot be found inherently.

Accordingly, Applicants respectfully request that the Examiner withdraw this rejection under 35 U.S.C. §102(b) and allow claims 2, 4, 8, 9, 28, 29, 30, 41, 43-49 and 50.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance, and notification to that effect is earnestly requested. The Examiner is invited to telephone the undersigned at (516) 795-6820 to facilitate prosecution of this application.

If necessary, please charge any additional fees or deficiencies, or credit any overpayments to Deposit Account No. 19-0743.

Respectfully submitted,

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Date February 1, 2011

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being filed using the USPTO's electronic filing system EFS-Web, and is addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this 1st day of February, 2011.

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Signature